



(Billing Code: 4150-31)

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of the Secretary

Findings of Research Misconduct

AGENCY: Office of the Secretary, HHS

ACTION: Notice.

SUMMARY: Notice is hereby given that the Office of Research Integrity (ORI) has taken final action in the following case:

Paul J. Muchowski, Ph.D., The J. David Gladstone Institutes: Based on the report of an investigation conducted by The J. David Gladstone Institutes (Gladstone) and additional analysis conducted by ORI in its oversight review, ORI found that Dr. Paul J. Muchowski, former Senior Investigator, Gladstone Institute of Neurological Disease, Gladstone, engaged in research misconduct in research supported by National Institute of Neurological Diseases and Stroke (NINDS), National Institutes of Health (NIH), grant R01 NS054753-06A1.

ORI found that the Respondent engaged in research misconduct by falsifying and fabricating data that was included in one (1) funded NIH grant R01 NS054753-06A1 and two (2) submitted NIH grant applications R01 NS054753-06 and R01 NS047237-06.

Specifically, ORI finds that the Respondent knowingly and intentionally:

- falsely reported research experiments when the results did not exist at the time the grant applications were submitted. Specifically:
 - ▶ in Figures 19-21 and related text of grant application R01 NS047237-06, the Respondent claimed he had successfully transduced human neuroblastoma SH-SY5Y cells expressing α -synuclein (α Syn) with lentiviruses containing small hairpin RNAs (shRNAs) that targeted *Cog6*, *Stx7*, *Vps52*, or *Vps33a*. The Respondent reported lentiviral expressed *Cog6* significantly exacerbated α -Syn toxicity in SH-SY5Y cells, when only plasmid shRNAs were generated and utilized at the time the grant application was submitted.
 - ▶ in Figure 5 and the accompanying text of grant R01 NS054753-06A1, the Respondent described the insertion of toxic and inert mutant huntingtin (htt) fragments into maltose binding protein-Htt-Cerulean constructs with a nonpathogenic (25Q) or pathogenic (46Q) polyQ repeat, with and without Cerulean. The modified proteins were claimed to have been purified, when the constructs had not been made at the time the grant was submitted.
 - ▶ in Figures 5 and 6 and the accompanying text of grant R01 NS054753-06A1, the Respondent claimed to have cloned toxic and inert mutant htt fragments into lentiviral constructs and generated lentiviruses, when the constructs were not made.

- ▶ in Figure 6 and related text in grant R01 NS054753-06A1, the Respondent claimed to have tested immunoblots of lysates from primary neurons with an antibody against mutant htt, which demonstrated that levels of htt expression in transduced cells were roughly equivalent to levels in normal neurons, when the experiment was not conducted.
- falsified Figure 3 of grant application R01 NS054753-06 by labeling the Western blot images for the expression of mutant htt in lentiviral-transduced primary neurons as ‘Cortex’ (left panel) and ‘Striatum’ (right panel), when the results were actually from the microglial cell lines N9 and BV2, respectively.

Dr. Muchowski has entered into a Voluntary Settlement Agreement and has voluntarily agreed for a period of two (2) years, beginning on December 10, 2012:

- (1) to have his research supervised; Respondent agreed that prior to the submission of an application for PHS support for a research project on which his participation is proposed and prior to his participation in any capacity on PHS-supported research, Respondent shall ensure that a plan for supervision of his duties is submitted to ORI for approval; the supervision plan must be designed to ensure the scientific integrity of his research contribution; he agreed that he shall not participate in any PHS-supported research until such a supervision plan is submitted to and

approved by ORI; Respondent agreed to maintain responsibility for compliance with the agreed upon supervision plan; and

- (2) to exclude himself voluntarily from serving in any advisory capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant.

FOR FURTHER INFORMATION CONTACT:

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